Sub

```
wherein
```

Xis -O-, -S-, -NH-, [-N(R₂)] <u>or -N(R₂);</u>

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

 C_{10})cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy when p is 2 and X is -O-;

 $[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein}]$

 R_{20} is -(CH₂)_n- where] n is 2, 3, 4, or 5;

 $[R_{21} is$

-CH₂-CH=CH-CH₂-,

-CH₂-C =C-CH₂-,

 $-CH_2-CH=CH-CH_2-CH_2$,

-CH₂-CH₂-CH=CH-CH₂-,

-CH₂-C \equiv C-CH₂-CH₂-, or

-CH₂-CH₂-C \equiv C-CH₂,

the -CH=CH- bond being cis or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phonyl group, or

Bob CI

$$||(Z_1)_p||$$
 lower alkyleneyl

where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, p is as previously defined;]

R is hydrogen, lower alkyl lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,]

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or

-CH(OR₇)-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;]

alkyl is lower alkyl;

aryl is phenyl or

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

____Q₃

Sub

Q3 is -O-, -S-, -NH-, <u>or</u> -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

R₇ is hydrogen, lower alkyl, or [alkanoyl] <u>acyl;</u>

[R₈ is lower alkyl;

R₉ is hydroxy, alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁ C₃ acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;] and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or X Y is hydrogen, and R is hydrogen,

[C_1 =14 C_4] $\underline{C_1}$ - $\underline{C_4}$ alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy,

or -COOR₂₃ where R₂₃ is C₁-C₄ alkyl;

with the exclusion of compounds wherein X is -S-, $[R_1 \text{ is } R_{20}]$ R is H, and m=1;

[all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid

9. (Amended)

addition salt thereof.

A compound as claimed in claim 1, wherein X is -O-, S-, or -NH-;

Y is H, Cl, F. -CF₃; R is selected from the group consisting of hydrogen, C₁-C₃ alkyl, C₁-C₃

- alkoxy, -OH, CL, F, Br, I, [acyl,] C_1 - C_3 monoalkylamino, acylamino, [-NO₂-,] -NO₂, -OCF₃, -

CF₃; and n is 2, 3, or 4.

25\ (Twice Amended)

A compound of the formula:

B4 506

wherein

X is -O-, -S-, -NH-, $[-N-R_2]$ or $-N(R_2)$;

p is 1 or 2;

Y is hydrogen, Cl, Br, or F when p is 1;

Y is lower alkoxy[or halogen] when p is 2 and X is -O-;

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

C₁₀)cycloalkyl, aroyl, (C₂-C₁₁)alkanoyl, and phenylsulfonyl groups;

aryl is phenyl or

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

n is 2, 3, or 4;

B4 50 19 C3

R is hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl, [acyl, (C₂-C₁₁) alkanoyl,] Cl, F, Br,

I, amino, C₁-C₃ mono- or dialkylamino, acylamino, -NO₂, -OCF₃, -CF₃,

-C(=O)-alkyl, δr -CH(OR₇)-alkyl;

alkyl is lower alkyl;

R₇ is hydrogen, lower alkyl, or acyl; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

 C_1 - C_3 alkyl, chlorine, fluorine, bromine, iodine, or C_1 - C_3 alkoxy;

with the exclusion of compounds wherein X is -S-, R is H, and m=1;

or a pharmaceutically acceptable acid addition salt thereof.

26. (Twice Amended) A compound of the formula:

$$(Y)_{p} = \underbrace{ \begin{pmatrix} (R)_{m} \\ N - (CH_{2})_{nO} - \end{pmatrix} \end{pmatrix} \right)$$

wherein X is -O-;

p is 1 or 2;

Y is hydrogen, hydroxy, Cl, Br, or F, when p is 1;

Y is lower alkoxy[, hydroxy, or halogen] when p is 2;

n is 2, 3, or 4;

R is hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl, [acyl, (C₂-C₁₁) alkanoyl,] Cl, F, Br,

I, amino, C₁-C₃ mono- or dialkylamino, acylamino, -NO₂, -OCF₃, -CF₃,

-C(=O)-alkyl, or -CH(OR₇)-alkyl[,];

B4

alkyl is lower alkyl;

R₇ is hydrogen, lower alkyl, or acyl; and

m is 1, 2, or 3;

with the exclusion of compounds wherein Y is hydrogen, and R is hydrogen, C₁-C₃ alkyl,

chlorine, fluorine, bromine, iodine, or C₁-C₃ alkoxy;

or a pharmaceutically acceptable acid addition salt thereof.

27. (Twice Amended) A compound of the formula:

5 b

wherein X is -S-;

p is 1 [or 2];

Y is hydrogen, Cl, Br, or F[, when p is 1];

[Y is lower alkoxy or halogen when p is 2;]

n is 2, 3, or 4;

R is hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl, [acyl, (C₂-C₁₁) alkanoyl,] Cl, F, Br,

I, amino, C₁-C₃ mono- or dialkylamino, acylamino, -NO₂, -OCF₃, -CF₃,

-C(=O)-alkyl, or -CH(OR₇)-alkyl[,];

alkyl is lower alkyl;

R₇ is hydrogen, lower alkyl, or acyl; and

Sub CY

m is 1, 2, or 3;

with the exclusion of compounds wherein Y is hydrogen, and R is hydrogen, C₁-C₃ alkyl,

chlorine, fluorine, bromine, iodine, C₁-C₃ alkoxy;

with the exclusion of compounds wherein R is H, and m=1;

or a pharmaceutically acceptable acid addition salt thereof.

28. (Twice Amended) A compound of the formula:

wherein X is -NH-;

p is 1 [or 2];

Y is hydrogen, Cl, Br, or F[, when p is 1];

[Y is lower alkoxy or halogen when p is 2;]

n is 2, 3, or 4;

R is hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl, [acyl, (C₂-C₁₁) alkanoyl,] Cl, F, Br,

I, amino, C₁-C₃ mono- or dialkylamino, acylamino, -NO₂, -OCF₃, -CF₃,

-C(=O)-alkyl, or -CH(OR₇)-alkyl[,];

alkyl is lower alkyl;

R₇ is hydrogen, lower alkyl, or acyl; and

m is 1, 2, or 3;

or a pharmaceutically acceptable acid addition salt thereof.

 $\mathcal{B}^{\#}$

29.\ (Twice Amended)

A compound of the formula:

wherein X is -N-R₂;

p is 1 [or 2];

Y is hydrogen, Cl, Br, or F[, when p is 1];

[Y is lower alkoxy or halogen when p is 2;]

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

 C_{10})cycloalkyl, aroyl, (C_2-C_{11}) [aroyl,] alkanoyl, and phenylsulfonyl groups; aryl is phenyl or

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano,

 $trifluoromethyl,\, or\, trifluoromethoxy;\\$

n is 2, 3, or 4;

BH

Suh cs R is hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, hydroxyl, [acyl, (C₂-C₁₁) alkanoyl,] Cl, F, Br,

I, amino, C₁-C₃ mono- or dialkylamino, acylamino, -NO₂, -OCF₃, -CF₃,

-C(=0)-alkyl, or $-CH(OR_7)$ -alkyl[,];

alkyl is lower alkyl;

R₇ is hydrogen, lower alkyl, or acyl; and

m is 1, 2, or 3;

or a pharmaceutically acceptable acid addition salt thereof.

30. (Twice Amended) A pharmaceutical composition, which comprises a compound of the formula:

$$(Y)_{p} \longrightarrow (R)_{m}$$

$$(Y)_{p} \longrightarrow (R)_{m}$$

$$(Y)_{p} \longrightarrow (R)_{m}$$

$$(Y)_{p} \longrightarrow (R)_{m}$$

wherein

$$X \text{ is -O-, -S-, -NH-, or -N}(R_2);$$

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

C₁₀)cycloalkyl, aroyl, (C₂-C₁₁)alkanoyl, and phenylsulfonyl groups;

50h C5 where aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy when p is 2 and X is -O-;

 $[R_1 \text{ is } R_{20}, R_{21}]$ or R_{22} , wherein:

 R_{20} is -(CN₂)_n- where] n is 2, 3, 4, or 5;

 $[R_{21} is$

 $-CH_2-C=CH-CH_2-$

 $-CH_2-C \equiv C-CH_2-$

-CH₂-CH=CH-CH₂-CH₂,

 $-CH_2-CH_2-CH=CN-CH_2-$

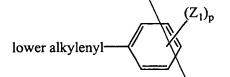
 $-CH_2-C = C-CH_2-CH_2 \setminus or$

-CH₂-CH₂-C ≡C-CH₂,

the -CH=CH- bond being ais or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted

by at least on C₁-C₆ linear alkyl group, phenyl group, or



where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂,-NH₂ or halogen, and p is as previously defined;]

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine,

50 b CS bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,]
-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or
-CH(OR₇)-alkyl, [-C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;]

alkyl is lower alkyl;

aryl is phenyl or

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

$$Q_3$$

Q₃ is -O-, -S-, -NH-, <u>or</u> -CH=N-;

[W is CH2 or CHR8 or N-R9;]

 R_7 is hydrogen, lower alkyl, or $[(C_2-C_{11})$ alkanoyl] <u>acyl</u>;

[R₈ is lower alkyl;

Sub

 R_9 is hydroxy, alkoxy, or -NHR₁₀; and

R₁₀\s hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

where aryl and heteroaryl are as defined above;] and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

 C_1 - C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy, or -COOR₂₃ where R_{23} is C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, $[R_1 \text{ is } R_{20},] R \text{ is H, and m=1};$

[all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid addition salt thereof, and a pharmaceutically acceptable carrier therefor.

31. (Twice Amended) An antipsychotic composition, which comprises a compound of the formula:

B

50b

wherein

X is -O-, S-, -NH-, or -N(R_2);

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

C₁₀)cycloalkyl, aroyl, (C₂-C₁₁)alkanoyl, and phenylsulfonyl groups;

where aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy when p is 2 and X is -O-;

 $[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein:}$

 R_{20} is -(CH₂)_n- where] n is 2, 3, 4, or 5;

 $[R_{21} is$

-CH₂-CH=CH-CH₂-,

-CH₂-C \equiv C-CH₂-,

-CH₂-CH=CH-CH₂-CH₂,

-CH₂-CH₂-CH=CH-CH₂-,

-CH₂-C \equiv C-CH₂-CH₂-, or

-CH₂-CH₂-C \equiv C-CH₂,

the -CH=CH- bond being cis or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least on C_1 - C_6 linear alkyl group, phenyl group, or

Suh Cs

lower alkylenyl
$$(Z_1)_p$$

where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, a p is as previously defined;]

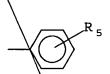
R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,]

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or

-CH(OR7)-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;]

alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is

Q₃ is -O-, -S-, -NH-, <u>or</u> -CH=N-;

Sub

[W\s CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or [(C_2 - C_{11}) alkanoyl] <u>acyl</u>;

[R₈ is lower alkyl;

 R_9 is hydrox alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-arylor -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;] and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C_1 - C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy, or -COOR₂₃ where R_{23} is C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, $[R_1 \text{ is } R_{20}]$ R is H, and m=1;

[all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid addition salt thereof, in an amount sufficient to produce an antipsychotic effect, and a pharmaceutically acceptable carrier therefor.

32. (Twice Amended) A method of treating psychoses, which comprises administering to a mammal a psychoses-treating effective amount of a compound of the formula:

50 b (5)

$$(X)^{b}$$

$$(X)^$$

wherein

X is -O-, -S-, -NH-, or - $N(R_2)$;

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

 C_{10})cycloalkyl, aroyl, (C_2 - C_{11})alkanoyl, and phenylsulfonyl groups;

where aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p\is 1;

Y is lower alkoxy when p is 2 and X is -O-;

 $[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein:}$

 R_{20} is -(CH₂)_n- where] n is 2, 3, 4, or 5;

 $[R_{21} is$

-CH₂-CH=CH-CH₂-,

-CH₂-C \equiv C-CH₂-,

Sub

-CH₂-CH=CH-CH₂-CH₂,
-CH₂-CH=CH-CH₂-,
-CH₂-C = C-CH₂-CH₂-, or
-CH₂-CH₂-C = C-CH₂,
the -CH=CH- bond being cis or trans;

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least on $C_1 \setminus C_6$ linear alkyl group, phenyl group, or

lower alkyleneyl (Z₁)_p

where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, and p is as previously defined.]

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,]

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or

-CH(OR₇)-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;]

alkyl is lower alkyl; aryl is phenyl or

34 50 h (5 where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano,

rifluoromethyl, or trifluoromethoxy;

heteroaryl is



 Q_3 is -O-, -S-, -NH-, $\underline{\text{or}}$ -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or $[(C_2-C_{11})$ alkanoyl] <u>acyl</u>;

[R₈ is lower alkyl;

R₉ is hydroxy, alkoxy, or -NHR₁₀;\and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroar\l,

where aryl and heteroaryl are as defined above;] and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is Q or S, Y is hydrogen, and R is hydrogen,

C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

where R₂₃ is C₁-C₄ alkyl;

with the exclusion of compounds wherein X is -S-, [R] is R_{20} , R is H, and m=1;

[all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid

addition salt thereof.

33. (Twice Amended) An analgesic composition, which comprises a compound of

the formula:

wherein

X is -O-, -S-, -NH-, or -N(R_2);

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

C₁₀)cycloalkyl, aroyl, (C₂-C₁₁)alkanoyl, and phenylsulfonyl groups;

where aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy,

trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy when p is 2 and X is -O-;

 $[R_1 \text{ is } R_{20}, R_{21} \text{ or } R_{22}, \text{ wherein:}$

84 5 ch cs

```
R<sub>20</sub> is -(CH<sub>2</sub>)<sub>n</sub>- where] n is 2, 3, 4, or 5;

[R<sub>21</sub> is -CH<sub>2</sub>-CH=CH-CH<sub>2</sub>-,

-CH<sub>2</sub>-CH=CH-CH<sub>2</sub>-,

-CH<sub>2</sub>-CH=CH-CH<sub>2</sub>-CH<sub>2</sub>,

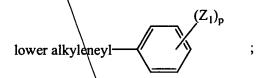
-CH<sub>2</sub>-CH=CH-CH<sub>2</sub>-,

-CH<sub>2</sub>-CH<sub>2</sub>-CH=CH-CH<sub>2</sub>-, or

-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, or

-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-bond being cis or trans;
```

 R_{22} is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least on C_1 - C_6 linear alkyl group, phenyl group, or



where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen, and p is as previously defined;]

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, [monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,]

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, or

-CH(OR7)-alkyl[,]; [-C(=W)-alkyl, -C(=W)-aryl, or-C(=W)-heteroaryl;]

Suh CS alkyl is lower alkyl;

aryl is phenyl or

where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine,

iodine, lower monoalkylamino, [lower dialkylamino,] nitro, cyano,

trifluoromethyl, or trifluoromethoxy;

heteroaryl is

Q₃ is -O-, -S-, -NH-, <u>or</u> -CH=N-;

[W is CH₂ or CHR₈ or N-R₉;]

 R_7 is hydrogen, lower alkyl, or $[(C_2 C_{11})$ alkanoyl] acyl;

[R₈ is lower alkyl;

R₉ is hydroxy, alkoxy, or -NHR₁₀; and

 R_{10} is hydrogen, lower alkyl, C_1 - C_3 acyl, arxl,

-C(=O)-aryl or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above;] and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

where R₂₃ is C₁-C₄ alkyl;

BYSUS

with the exclusion of compounds wherein X is -S-, $[R_1$ is R_{20} ,] R is H, and m=1; [all geometric, optical, and stereoisomers thereof,] or a pharmaceutically acceptable acid

addition salt thereof, in an amount sufficient to produce a pain-relieving effect,

34. (Amended) A method of alleviating pain, which comprises administering to a

mammal a pain-relieving effective amount of a [compound] composition as claimed in claim 33.

and a pharmaceutically acceptable carrier therefor.

Please replace claims 46, 54, 66, 74, 86-89, 92, 93, 96, and 104, all added by Preliminary Amendment dated November 9, 2000, with the following:

46. A compound of the formula

B5

$$(Y)_{p} \underbrace{\hspace{1cm} N - (R_{1}) - O}_{X} \underbrace{\hspace{1cm} N - (R_{1})}_{N} \underbrace{\hspace{1cm} N - (R_{1}) - O}_{N} \underbrace{\hspace{1cm} N - (R_{1})}_{N} \underbrace{\hspace{1cm} N - (R_{1})}_{N}$$

wherein

X is -O-, -S-, -NH-, or - $N(R_2)$;

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

B5

 $\underline{C_{10}}$)cycloalkyl, aroyl, $(\underline{C_2}-\underline{C_{11}})$ alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is

-CH2-CH=CH-CH2-,

 $-CH_2-C = C-CH_2-$

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C \equiv C-CH_2-$

the -CH=CH- bond being cis or trans;

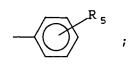
R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,

 $-CH(OR_7)$ -alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



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where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is



where Q₃ is -O-, -S-, -NH-, or -CH=N-;

 \underline{W} is $\underline{CH_2}$ or $\underline{CHR_8}$ or $\underline{N-R_9}$;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,



 C_1 - C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy, or -COOR₂₃ where R_{23} is C_1 - C_4 alkyl;

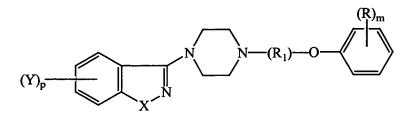
all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid addition salt thereof.

B 6

54. A compound as claimed in claim 46, wherein X is -O-, -S-, or -NH-; Y is H, Cl, F, -CF₃; R is selected from the group consisting of hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, -OH, Cl, F, Br, I, C₁-C₃ monoalkylamino, acylamino, -NO₂-, -OCF₃, -CF₃.

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66. A compound of the formula



wherein

X is -O-, -S-, -NH-, or -N(R₂);

 $\underline{R_2}$ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, ($\underline{C_3}$ -

 C_{10})cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

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p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group or

where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen;

 R_{20} is -(CH₂)_n-, where n is 2, 3, 4 or 5;

 R_{21} is

-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-$

-CH2-CH=CH-CH2-CH2-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C = C-CH_2-$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl,



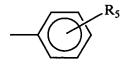
aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,

-CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is



where Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C_1 - C_3 acyl, aryl, -C(=O)-aryl, or -C(=O)-heteroaryl,

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where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

where R₂₃ is C₁-C₄ alkyl;

with the exclusion of compounds wherein X is -S-, R₁ is R₂₀, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

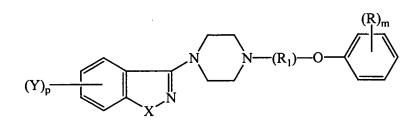
addition salt thereof.

B 8

74. A compound as claimed in claim 66, wherein X is -O-, -S-, or -NH-; Y is H, Cl, F, -CF₃; R is selected from the group consisting of hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, -OH, Cl, F, Br, I, C₁-C₃ monoalkylamino, acylamino, -NO₂, -OCF₃, -CF₃; and n is 2, 3, or 4.

BB

86. A pharmaceutical composition, which comprises a compound of the formula



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wherein

X is -O-, -S-, -NH-, or - $N(R_2)$;

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

C₁₀)cycloalkyl, aroyl, (C₂-C₁₁)alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

(R_1) is

-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-$,

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C$ \equiv C-CH₂-,

the -CH=CH- bond being cis or trans;

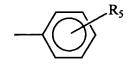
aminocarbonyl, dialkylaminocarbonyl, formyl,

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl,

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,
-CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



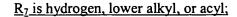
where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is



where Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH2 or CHR8 or N-R9;



R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C_1-C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1-C_4 alkoxy, or $-COOR_{23}$ where R_{23} is C_1-C_4 alkyl;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, and a pharmaceutically acceptable carrier therefor.

87. A pharmaceutical composition, which comprises a compound of the formula

$$(Y)_{p} \underbrace{\hspace{1cm} N \hspace{1cm} (R)_{m}}_{X} N \underbrace{\hspace{1cm} N \hspace{1cm} (R_{1}) \hspace{1cm} O \hspace{1cm} \underbrace{\hspace{1cm} (R)_{m}}_{M}}_{N}$$

wherein

X is -O-, -S-, -NH-, or -N(R_2);

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

C₁₀)cycloalkyl, aroyl, (C₂-C₁₁)alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group or

lower alkyleneyl
$$(Z_1)_p$$

where Z₁ is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen;

 R_{20} is -(CH₂)_n-, where n is 2, 3, 4 or 5;

 R_{21} is

-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-$

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

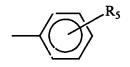
-CH2-CH2-C =C-CH2-,

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl, -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, -CH(OR7)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is



where Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH2 or CHR8 or N-R9;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, C_1 - C_4 alkyl, chlorine, fluorine, bromine, iodine, cyano, C_1 - C_4 alkoxy, or -COOR₂₃ where R_{23} is C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, R₁ is R₂₀, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, and a pharmaceutically acceptable carrier therefor.

88. An antipsychotic composition, which comprises a compound of the formula

wherein

 $X \text{ is -O-, -S-, -NH-, or -N(R}_2);$

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

 $\underline{C_{10}}$)cycloalkyl, aroyl, $(\underline{C_2}$ - $\underline{C_{11}}$)alkanoyl, and phenylsulfonyl groups;

aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is

-CH2-CH=CH-CH2-,

-CH₂-C =€-CH₂-,

-CH₂-CH=CH-CH₂-CH₂-,

 $-CH_2-CH_2-CH=CH-CH_2-$

 $-CH_2-C = C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C = C-CH_2-$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, dialkylaminocarbonyl, formyl,

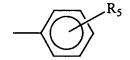
-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,

-CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or

 \mathcal{B}^{g}



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is



where Q₃ is -O-, -S-, -NH-, or -CH=N-;

W is CH2 or CHR8 or N-R9;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

where R₂₃ is C₁-C₄ alkyl;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, in an amount sufficient to produce an antipsychotic effect,

and a pharmaceutically acceptable carrier therefor.

89. An antipsychotic composition, which comprises a compound of the formula

$$(Y)_{p} \underbrace{\hspace{1cm} N - (R_{1}) - O}_{X} \underbrace{\hspace{1cm} N}_{N} \underbrace{\hspace{1cm} N - (R_{1}) - O}_{N} \underbrace{\hspace{1cm} N}_{N} \underbrace{\hspace{1cm} N} \underbrace{\hspace{1cm} N}_{N} \underbrace{\hspace{1cm} N}_{N} \underbrace{\hspace{1cm} N}_{N} \underbrace{\hspace{1cm} N}$$

wherein

 $X \text{ is -O-, -S-, -NH-, or -N(R}_2);$

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, $(C_3$ - C_{10})cycloalkyl, aroyl, $(C_2$ - C_{11})alkanoyl, and phenylsulfonyl groups; aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

(R_1) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group or



lower alkyleneyl
$$(Z_1)_p$$

where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen;

 R_{20} is -(CH₂)_n-, where n is 2, 3, 4 or 5;

 R_{21} is

-CH2-CH=CH-CH2-,

 $-CH_2-C = C-CH_2-$

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C$ \equiv C-CH₂-CH₂-, or

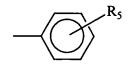
 $-CH_2-CH_2-C = C-CH_2-$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl, -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl, -CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



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where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is



where Q₃ is -O-, -S-, -NH-, or -CH=N-;

W is CH2 or CHR8 or N-R9;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

89

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

where R₂₃ is C₁-C₄ alkyl;

with the exclusion of compounds wherein X is -S-, R₁ is R₂₀, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof, in an amount sufficient to produce an antipsychotic effect,

and a pharmaceutically acceptable carrier therefor.

B10

92. An analgesic composition, which comprises a compound of the formula

wherein

X is -O-, -S-, -NH-, or -N(R_2);

R₂ is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C₃-

 C_{10})cycloalkyl, aroyl, (C_2-C_{11}) alkanoyl, and phenylsulfonyl groups; aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy,

trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is

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-CH2-CH=CH-CH2-,

 $-CH_2-C = C-CH_2-$

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C = C-CH_2-$

the -CH=CH- bond being cis or trans;

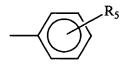
R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl, aminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-heteroaryl,

-CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine,

iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is

B 10



where Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

Ro is hydroxy, lower alkoxy, or -NHR10; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen, $C_1-C_4 \text{ alkyl, chlorine, fluorine, bromine, iodine, cyano, } C_1-C_4 \text{ alkoxy, or -COOR}_{23}$ where R_{23} is C_1-C_4 alkyl;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid addition salt thereof, in an amount sufficient to produce a pain-relieving effect,

and a pharmaceutically acceptable carrier therefor.

93. An analgesic composition, which comprises a compound of the formula

 \mathcal{B}^{10}

wherein

 $X \text{ is -O-, -S-, -NH-, or -N(R}_2);$

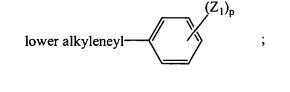
 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, (C_3 - C_{10})cycloalkyl, aroyl, (C_2 - C_{11})alkanoyl, and phenylsulfonyl groups; aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

 (R_1) is R_{20} or R_{21} in which one or more carbon atoms of R_{20} or R_{21} are substituted by at least one C_1 - C_6 linear alkyl group, phenyl group or



where Z_1 is lower alkyl, -OH, lower alkoxy, -CF₃, -NO₂, -NH₂ or halogen; R_{20} is -(CH₂)_n-, where n is 2, 3, 4 or 5;

<u>R₂₁ is</u>

-CH₂-CH=CH-CH₂-,

 $-CH_2-C = C-CH_2-$

-CH₂-CH=CH-CH₂-CH₂-,

-CH₂-CH₂-CH=CH-CH₂-,

 $-CH_2-C \equiv C-CH_2-CH_2-$, or

 $-CH_2-CH_2-C = C-CH_2-$

the -CH=CH- bond being cis or trans;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine,

iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio,

trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl,

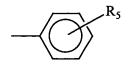
aminocarbonyl, monoalkylaminocarbonyl, dialkylaminocarbonyl, formyl,

-C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-aryl, -C(=O)-heteroaryl,

-CH(OR₇)-alkyl, -C(=W)-alkyl, -C(=W)-aryl, or -C(=W)-heteroaryl;

where alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine,

iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, trifluoromethoxy;

heteroaryl is

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where Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl, or -C(=O)-heteroaryl,

where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

where R_{23} is C_1 - C_4 alkyl;

with the exclusion of compounds wherein X is -S-, R₁ is R₂₀, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

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addition salt thereof, in an amount sufficient to produce a pain-relieving effect, and a pharmaceutically acceptable carrier therefor.

96. A compound of the formula

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wherein

X is -O-, -S-, -NH-, or -N(R_2);

 R_2 is selected from the group consisting of lower alkyl, aryl lower alkyl, aryl, $(C_3$ - C_{10})cycloalkyl, aroyl, $(C_2$ - C_{11})alkanoyl, and phenylsulfonyl groups; aryl is as defined hereinafter;

p is 1 or 2;

Y is hydrogen, lower alkyl, hydroxy, chlorine, fluorine, bromine, iodine, lower alkoxy, trifluoromethyl, nitro, or amino, when p is 1;

Y is lower alkoxy, hydroxy, or halogen when p is 2 and X is -O-;

n is 2, 3, 4 or 5;

R is hydrogen, lower alkyl, lower alkoxy, hydroxyl, carboxyl, chlorine, fluorine, bromine, iodine, amino, lower mono or dialkylamino, nitro, lower alkyl thio, trifluoromethoxy, cyano, acylamino, trifluoromethyl, trifluoroacetyl,

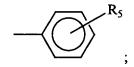
<u>aminocarbonyl, dialkylaminocarbonyl, formyl, -C(=O)-alkyl, -C(=O)-O-alkyl, -C(=O)-alkyl, -C(=O)-heteroaryl, -CH(OR₇)-alkyl, -C(=W)-alkyl,</u>

-C(=W)-aryl, or -C(=W)-heteroaryl;

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alkyl is lower alkyl;

aryl is phenyl or



where R₅ is hydrogen, lower alkyl, lower alkoxy, hydroxy, chlorine, fluorine, bromine, iodine, lower monoalkylamino, lower dialkylamino, nitro, cyano, trifluoromethyl, or trifluoromethoxy;

heteroaryl is



 Q_3 is -O-, -S-, -NH-, or -CH=N-;

W is CH₂ or CHR₈ or N-R₉;

R₇ is hydrogen, lower alkyl, or acyl;

R₈ is lower alkyl;

R₉ is hydroxy, lower alkoxy, or -NHR₁₀; and

R₁₀ is hydrogen, lower alkyl, C₁-C₃ acyl, aryl,

-C(=O)-aryl or -C(=O)-heteroaryl,

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where aryl and heteroaryl are as defined above; and

m is 1, 2, or 3;

with the proviso that at least one R is selected from the group consisting of

dialkylaminocarbonyl, formyl, -C(=W)-alkyl, -C(=W)-aryl, and

-C(=W)-heteroaryl;

with the exclusion of compounds wherein X is O or S, Y is hydrogen, and R is hydrogen,

C₁-C₄ alkyl, chlorine, fluorine, bromine, iodine, cyano, C₁-C₄ alkoxy, or -COOR₂₃

where R₂₃ is C₁-C₄ alkyl;

with the exclusion of compounds wherein X is -S-, R is H, and m=1;

all geometric, optical and stereoisomers thereof, or a pharmaceutically acceptable acid

addition salt thereof.

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104. A compound as claimed in claim 96, wherein X is -O-, -S-, or -NH-; Y is H, Cl, F, -CF₃; R is selected from the group consisting of hydrogen, C₁-C₃ alkyl, C₁-C₃ alkoxy, -OH, Cl, F, Br, I, C₁-C₃ monoalkylamino, acylamino, -NO₂, -OCF₃, -CF₃; and n is 2, 3, or 4.

REMARKS

In this amendment, Patent Owner has amended claims 1, 9, 25-33, 46, 54, 66, 74, 86-89, 92, 93, 96, and 104, and cancelled claims 49 and 57. Claims 46-115 were added by Preliminary Amendment dated November 9, 2000. Thus, claims 1-48, 50-56, and 58-115 are pending.

The Examiner has indicated that claims 1-13 and 25-115 are rejected and that claims 14-